

## REMARKS

By this amendment, claim 1 is amended to explicitly recite the hand of man and to clarify that the protein encoded by the nucleic acid portion designated "protein(Y)" is selected from the group consisting of mini-proinsulin and proinsulin. Claims 1, 6-12 and 27-29 are pending. No issue of new matter arises.

Applicant gratefully acknowledges that only rejections under 35 USC §101 and 35 USC §112 (and one provisional rejection) remain to be overcome.

### **1) Rejections under 35 U.S.C. §112, first paragraph**

Rejection of claims 1-3 and 6-12 was maintained under 35 U.S.C. §112, first paragraph as allegedly failing to meet written description and enablement requirements. Applicant respectfully traverses these rejections.

#### ***Written Description***

The basis of this rejection appears to be that the claims do not recite "any functional characteristics". Office Action, page 4 line 18. The Office Action alleges that the claims recite a structure without any particular function. The Office Action recommends including language pertaining to functional characteristics of the genus. Applicant respectfully submits that such functional limitations are already present. Claim 1, paragraph 13 is also amended to more clearly indicate functionality. For example, claim 1, paragraphs 3 and 4, recite:

the nucleic acid codes for a fusion protein comprising a peptide encoded by transport peptide linked via a peptide encoded by a first  $Z_1Z_2$  to a protein encoded by said protein(Y) which is linked to T;

the peptide encoded by transport peptide improves the rate of secretion of the protein encoded by said protein(Y);

The nucleic acid has a recited function of coding for a fusion protein. Hirudin, encoded by the transport peptide, (see claim 1, paragraph 10) has a function of improving rate of secretion of mini-proinsulin or proinsulin, encoded by the nucleic acid fragment designated "protein Y". See, e.g., the specification page 2, lines 1 and 2: "Surprisingly, hirudin thus acts

as a kind of enhancer peptide with respect to the yield of mini-proinsulin.” Claim 1, thus as now written, clearly includes functional characteristics. The Examiner is respectfully requested to suggest any additional functional characteristics that might more fully describe the instantly claimed invention. Reconsideration and withdrawal of this rejection of claim 1 are respectfully requested.

Claims 6-12 and 27-29 ultimately depend from claim 1 and thus claim inventions that further limit the invention properly claimed in claim 1. Accordingly, reconsideration and withdrawal of this rejection of all claims are respectfully requested.

### ***Enablement***

The Office Action at page 5, lines 4 and 3 from bottom, states: “As stated above, applicants’ recitation of ‘transport peptide’ is merely to indicate a variable component wherein many different peptides may be used.” Applicant respectfully submits that indeed many hirudins including variants (encoded by “transport peptide”) exist. See, for example, the paragraph bridging pages 5 and 6 of the specification. This limited set of transport peptides poses no requirement for undue experimentation and therefore is clearly enabled. See also the referenced application, DE 3 430 556. Accordingly, the genus of this claim element is clearly enabled in the art.

The Office Action acknowledges: “A person of skill in the art would most probably be able to make the claimed genus, but would not be able to determine whether each species will retain the specific intended function (this being especially worrisome since there are no functional limitations in the claim).”

Applicant respectfully submits that the enablement requirement has been characterized as relying on a test of whether “undue experimentation” would have been required. As discussed above and below, no undue experimentation is implicated for practicing the instantly claimed invention. Applicant further respectfully submits that as described above, functional characteristics or limitations are features in the claims. This basis of rejection is thereby obviated or mooted.

As acknowledged in the Office Action no “undue experimentation” would be expected for the skilled artisan to make the claimed invention. The rejection must therefore rely on an allegation that the skilled artisan would require undue experimentation in order to use the

claimed invention. The Office Action in this rejection, sheds light on the misapplication of the statute and caselaw. At page 6, line 4, the Office Action references an “undue burden”. This will be interpreted by Applicant to mean “undue experimentation” since “undue burden” has no place in the applicable law.

The Action states: “Therefore the Examiner still believes that it is considered to be an undue burden for a person skill in the art to test all the possible constructs that are represented by the claimed structural formula.” Applicant respectfully submits that claims recite a chemical construct and do not recite that all embodiments of the construct must be made. Nowhere does any claim require testing “all the possible constructs”. According to 35 USC §112, the claimed invention must indeed be enabled. However, the enablement requirement pertains to each embodiment, the test being: Would undue experimentation be required for the skilled artisan to practice any one embodiment? (Inoperative embodiments are permitted so long as they may be discarded without undue experimentation.) In the present circumstance Applicant respectfully submits that for any one embodiment, only routine, not undue, experimentation would be required to practice the invention. As acknowledged above, “Making” is not an issue. To practice the invention, i.e., using the nucleic acid, the skilled artisan needs only routine laboratory practice to insert the nucleic acid into a host cell. Fermentation is also routine. See, for example, Example 4. Separation of protein components is also routine. See, for example, Example 6. If the skilled artisan is curious and wants to confirm benefits of practicing this invention, it would only be routine to construct a nucleic acid, for example without the “transport protein” component. Thus “improved rate of secretion” can be confirmed. Clearly no undue experimentation would have been required to practice the claimed invention.

The Office Action also includes another basis for this rejection: “There is no information in the claims or in the specification that would explain to a person skill in the art as to which portion of the construct is essential for the intended function characteristics- and in a nutshell this is the Patent Offices’ understanding of the ‘structure-function relationship’.” Applicant respectfully traverses this basis of rejection. For example, the structure of the nucleic acid segment “protein(Y)” has a function of encoding a protein selected from the group consisting of mini-proinsulin and proinsulin; the function of “transport peptide” is to encode hirudin or an hirudin variant; Px, Sx, Bn, Z, and R have known structures associated with their respective functions. For example, R, an arginine codon, by definition encodes for the amino

acid, arginine. Its structure is obtainable from many molecular biology sources and is known to be, for RNA, aga, agg, cgu, cgc cga or cgg or the corresponding DNA codon. Such well known, structure-function relationships should not have to be repeated in every patent application. Accordingly, despite allegations to the contrary in the Office Action, a review of the specification and art unambiguously reveals that structure of the various claim elements is indeed correlated with understood function. Reconsideration and withdrawal of this aspect of the rejection are respectfully requested.

Claims 6-12 and 27-29 ultimately depend from claim 1 and thus claim inventions that further limit the invention claimed in claim 1. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

### **2) Rejection under 35 USC §101 - Non-Statutory Subject Matter**

Claims 8, 11 and 12 were rejected as reciting non-statutory subject matter. Claim 1 is amended to explicitly recite "An article of manufacture" to "clearly implicate the hand of man". Claims 8, 11 and 12 ultimately depend from claim 1 and thus include this "hand of man" is included by reference in these rejected claims. The Office Action, at page 9, alleged as a basis for the rejection, "Peptides with good transport activity are available in nature and can be expressed in HOST CELLS with no hand of man." Applicant respectfully submits that this allegation is not relevant to the claimed invention. "Peptides with good transport activity" indeed exist in nature, but the claims do not simply claim "Peptides with good transport activity". Claim 1 recites a nucleic acid sequence of multiple elements, one of which is a transport peptide. For at least these reasons, reconsideration and withdrawal of this rejection are respectfully requested.

### **3) Provisional Double Patenting Rejections**

Claim 1 was provisionally rejected under a judicially created concept of double patenting. If still proper, Applicant will take appropriate action, such as an amendment or other action in this or 10/076,634 if and when claims are finalized by indication of allowable claimed subject matter.

### Conclusion

In view of the above amendments and remarks, Applicant respectfully requests reconsideration and withdrawal of all pending rejections. Applicant respectfully submits that the application is now in condition for allowance and request prompt issuance of a Notice of Allowance. Should the Examiner believe that anything further is desirable that might put the application in even better condition for allowance, the Examiner is requested to contact the undersigned at the telephone number listed below.

### Fees

No fees are believed to be necessitated by the instant response. However, should this be in error, authorization is hereby given to charge Deposit Account no. 18-1982 for any underpayment, or to credit any overpayments.

Respectfully submitted,



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